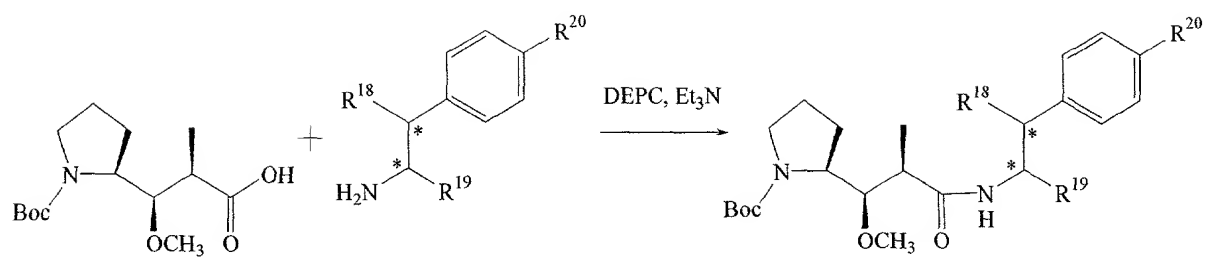


*Fig. 1*



*t*-Boc Dolaproine (**20**)

(**21**) (1*S*,2*R*) R<sup>18</sup>=OH, R<sup>19</sup>=Me, R<sup>20</sup>=H

(**22**) (*S*) R<sup>18</sup>=H, R<sup>19</sup>=CH<sub>2</sub>OH, R<sup>20</sup>=H

(**23**) (*R*) R<sup>18</sup>=H, R<sup>19</sup>=CH<sub>2</sub>OH, R<sup>20</sup>=H

(**24**) R<sup>18</sup>=H, R<sup>19</sup>=H, R<sup>20</sup>=C(O)CH<sub>3</sub>

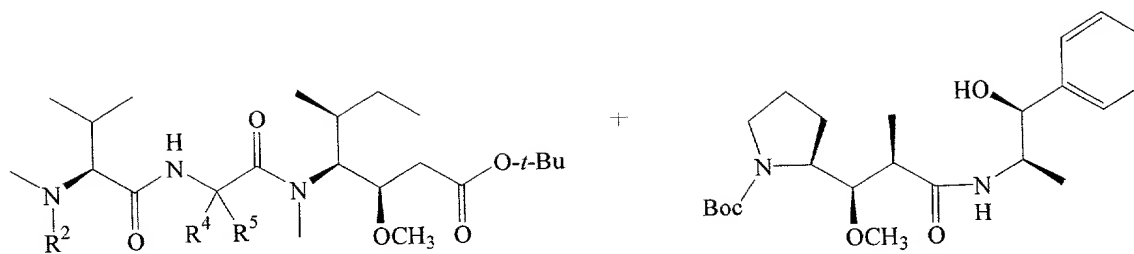
(**25**) (1*S*, 2*R*) R<sup>18</sup>=OH, R<sup>19</sup>=Me, R<sup>20</sup>=H

(**26**) (*S*) R<sup>18</sup>=H, R<sup>19</sup>=CH<sub>2</sub>OH, R<sup>20</sup>=H

(**27**) (*R*) R<sup>18</sup>=H, R<sup>19</sup>=CH<sub>2</sub>OH, R<sup>20</sup>=H

(**28**) R<sup>18</sup>=H, R<sup>19</sup>=H, R<sup>20</sup>=C(O)CH<sub>3</sub>

*Fig. 2*



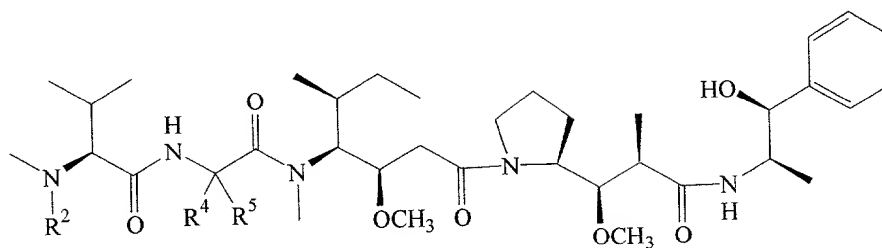
(18a)  $R^2 = \text{Me}$ ,  $R^4 = i\text{-propyl}$ ,  $R^5 = \text{H}$ ;

(18b)  $R^2 = \text{Me}$ ,  $R^4 = \text{sec-butyl}$ ,  $R^5 = \text{H}$ ;

(19a)  $R^2 = \text{Fmoc}$ ,  $R^4 = i\text{-propyl}$ ,  $R^5 = \text{H}$ ;

(19b)  $R^2 = \text{Fmoc}$ ,  $R^4 = \text{sec-butyl}$ ,  $R^5 = \text{H}$ ;

1. TFA/ $\text{CH}_2\text{Cl}_2$   
2. DEPC,  $\text{Et}_3\text{N}$  or,  
PyBrop,  $\text{EtN}(i\text{-Pr})_2$



(29a, auristatin E)  $R^2 = \text{Me}$ ,  $R^4 = i\text{-propyl}$ ,  $R^5 = \text{H}$ ;

(29b)  $R^2 = \text{Me}$ ,  $R^4 = \text{sec-butyl}$ ,  $R^5 = \text{H}$ ;

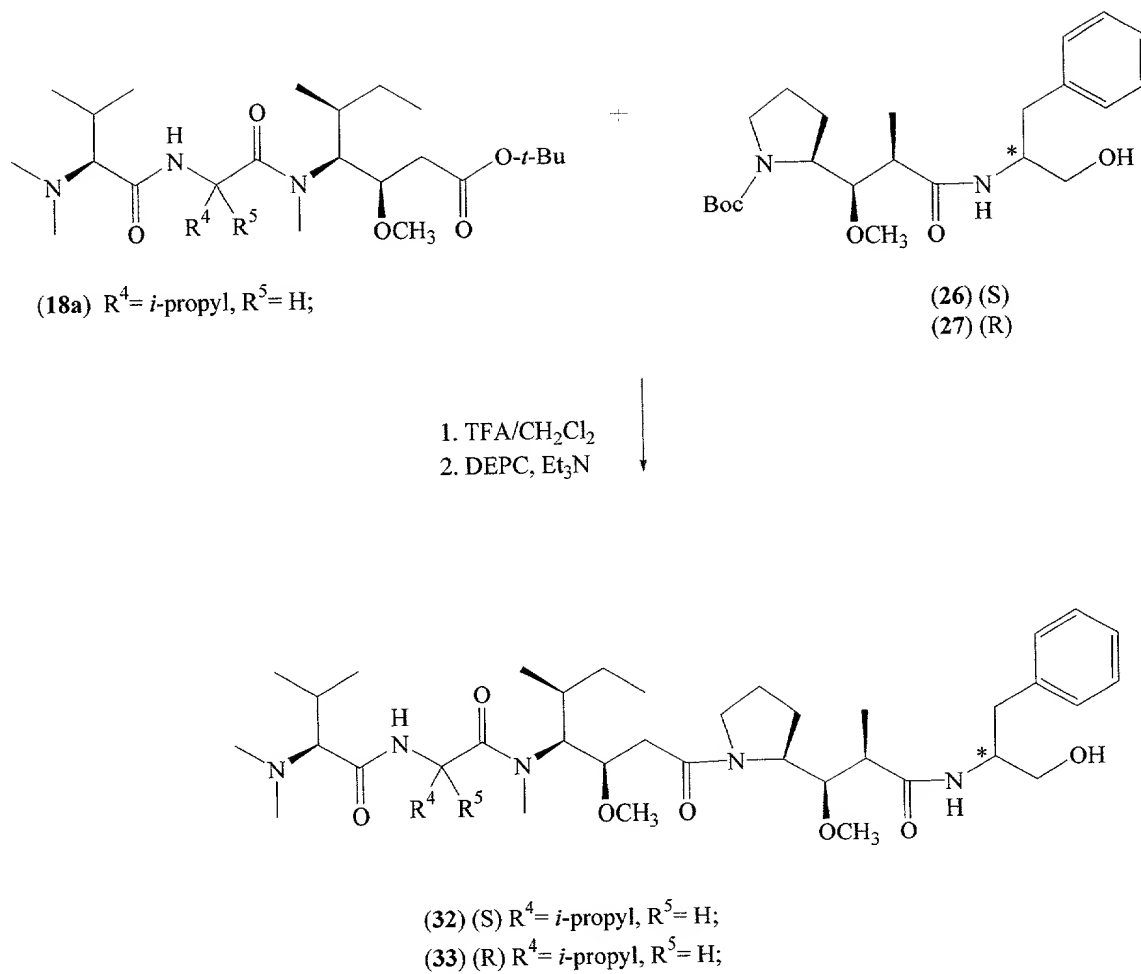
(30a)  $R^2 = \text{Fmoc}$ ,  $R^4 = i\text{-propyl}$ ,  $R^5 = \text{H}$ ;

- Fmoc  $\rightarrow$  (31a)  $R^2 = \text{H}$ ,  $R^4 = i\text{-propyl}$ ,  $R^5 = \text{H}$ ;

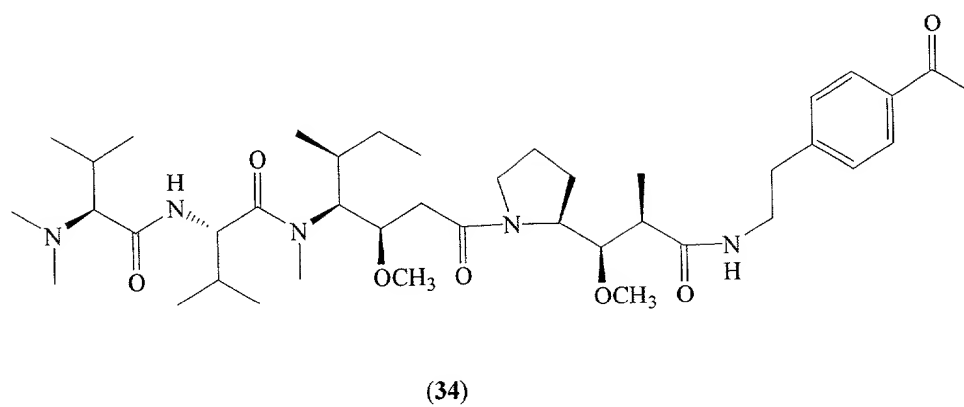
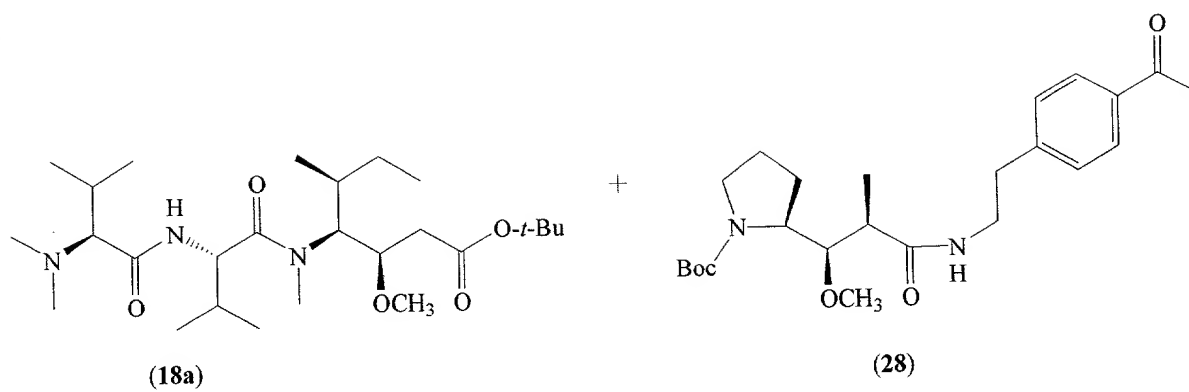
(30b)  $R^2 = \text{Fmoc}$ ,  $R^4 = \text{sec-butyl}$ ,  $R^5 = \text{H}$ ;

- Fmoc  $\rightarrow$  (31b)  $R^2 = \text{H}$ ,  $R^4 = \text{sec-butyl}$ ,  $R^5 = \text{H}$ ;

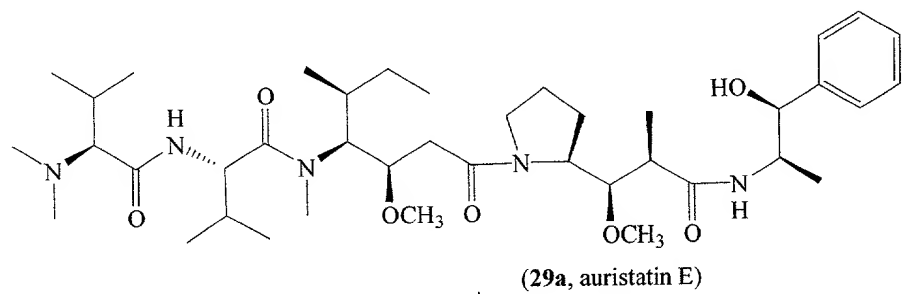
Fig. 3



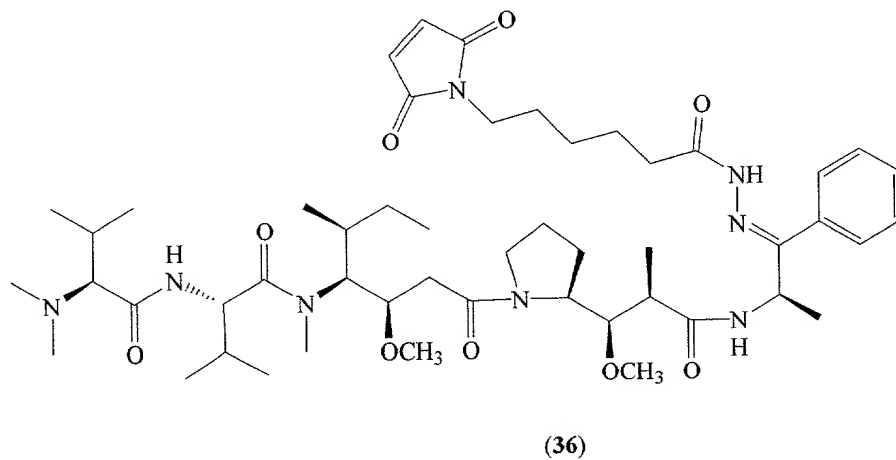
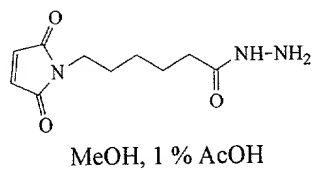
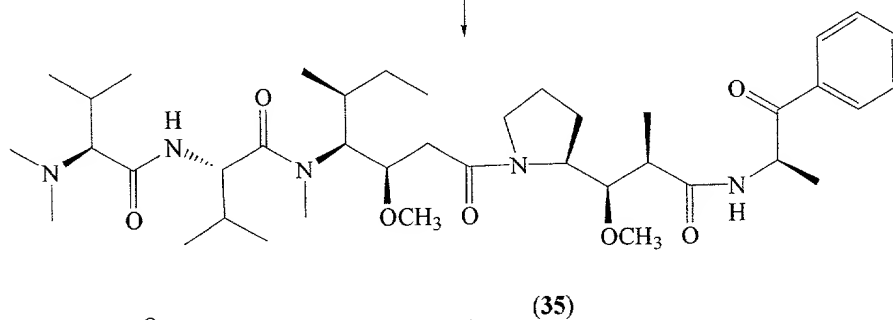
*Fig. 4*



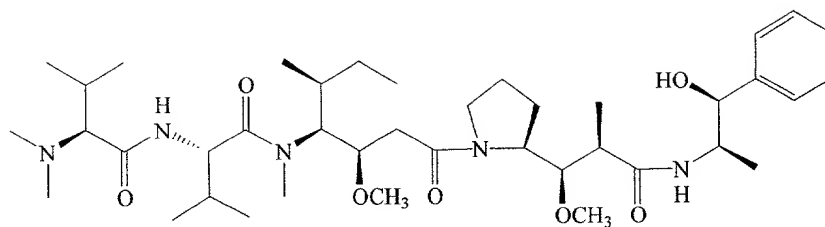
*Fig. 5*



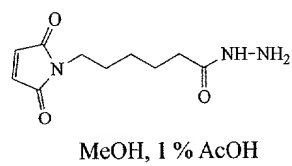
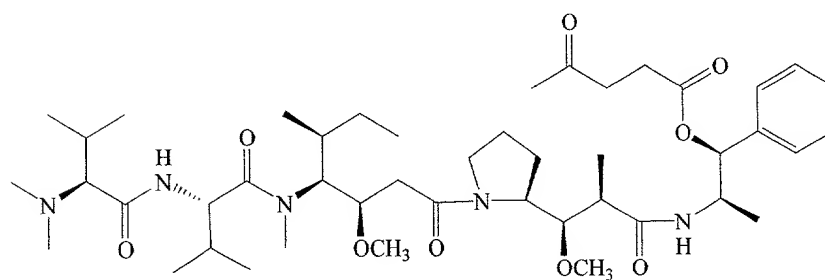
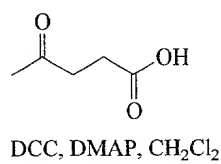
PCC, Py  
CH<sub>2</sub>Cl<sub>2</sub>



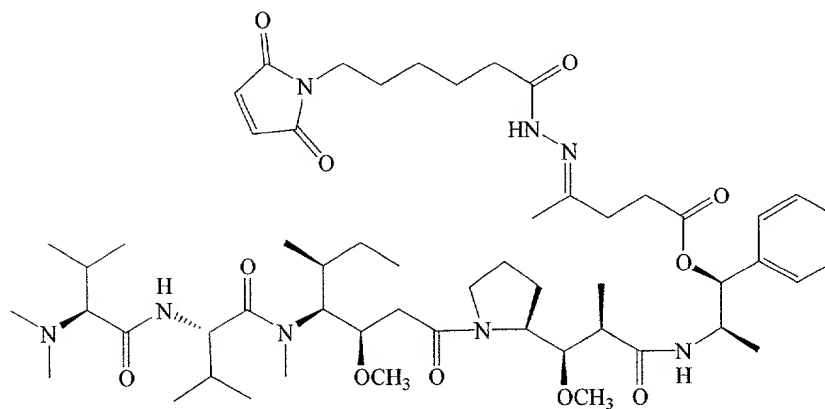
*Fig. 6*



(29a, auristatin E)



(37)



(38)

*Fig. 7*

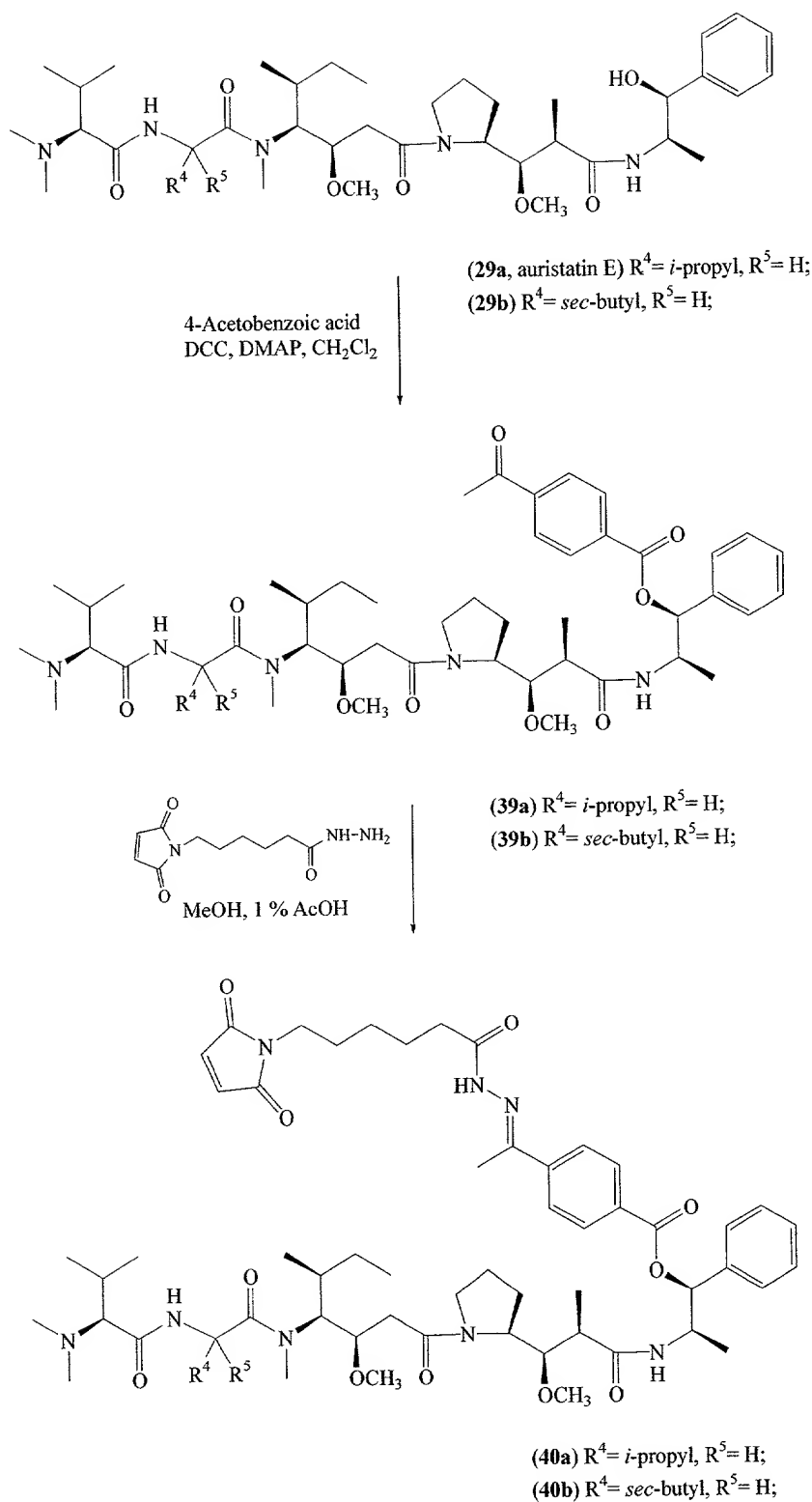
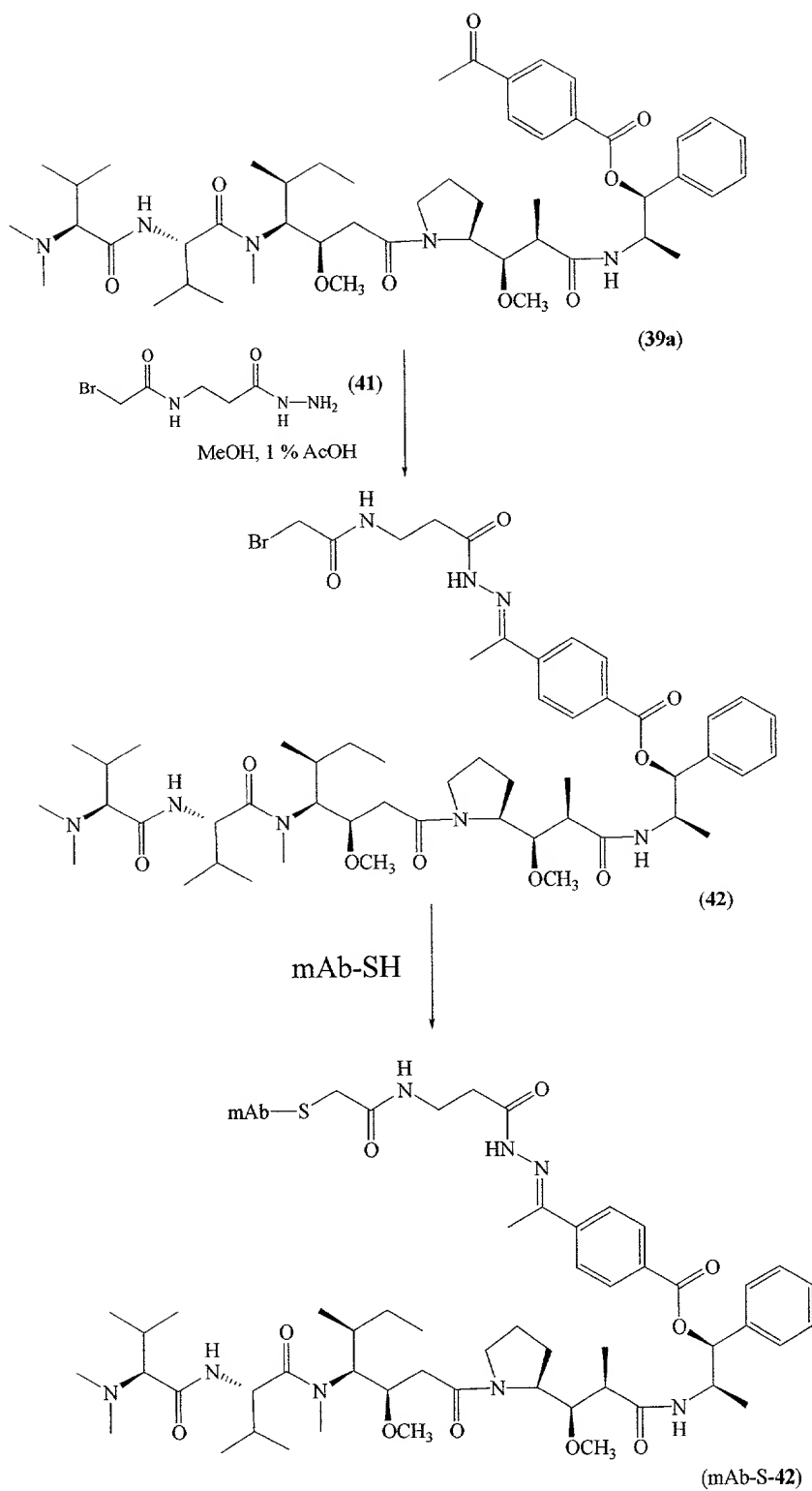
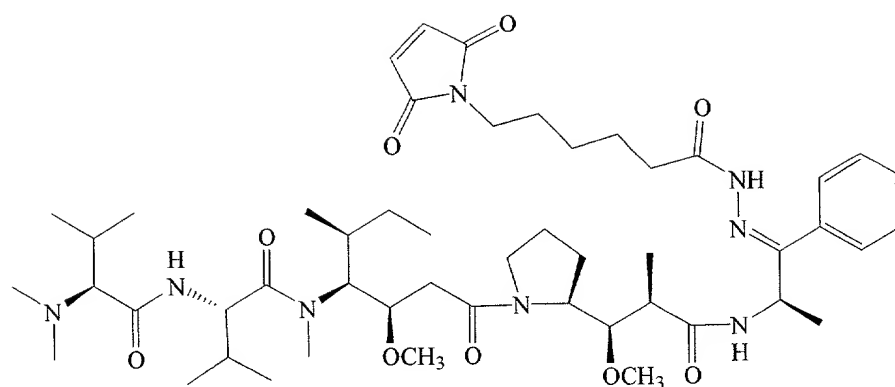


Fig. 8



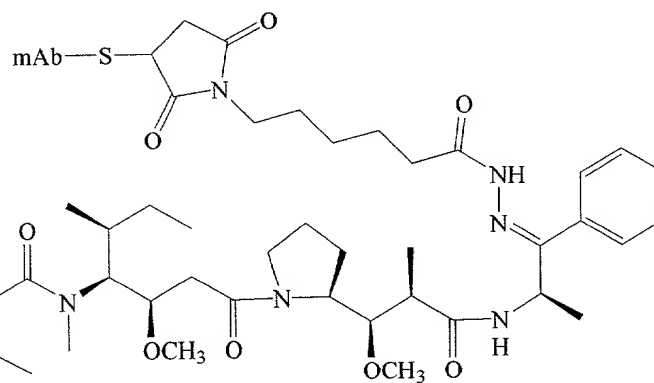


*Fig. 9*



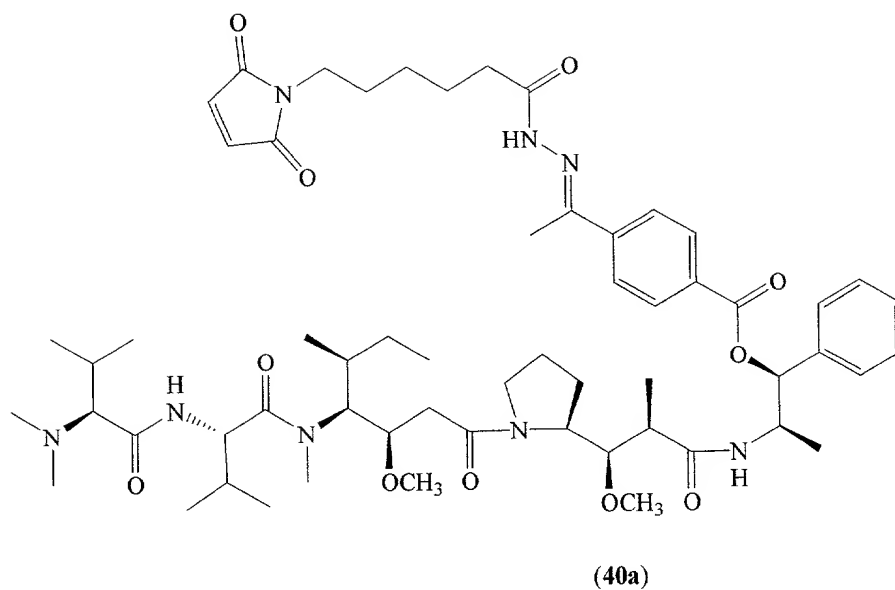
(36)

mAb-SH

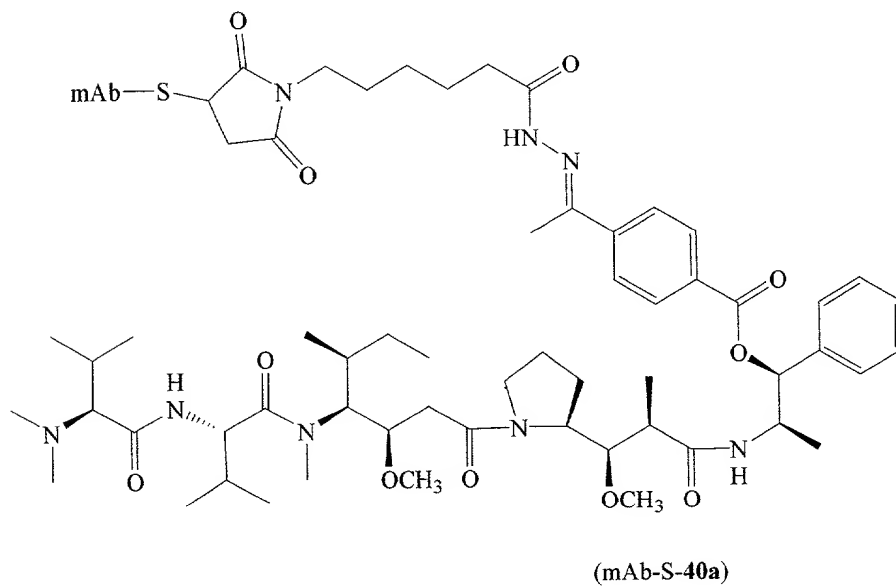


(mAb-S-36)

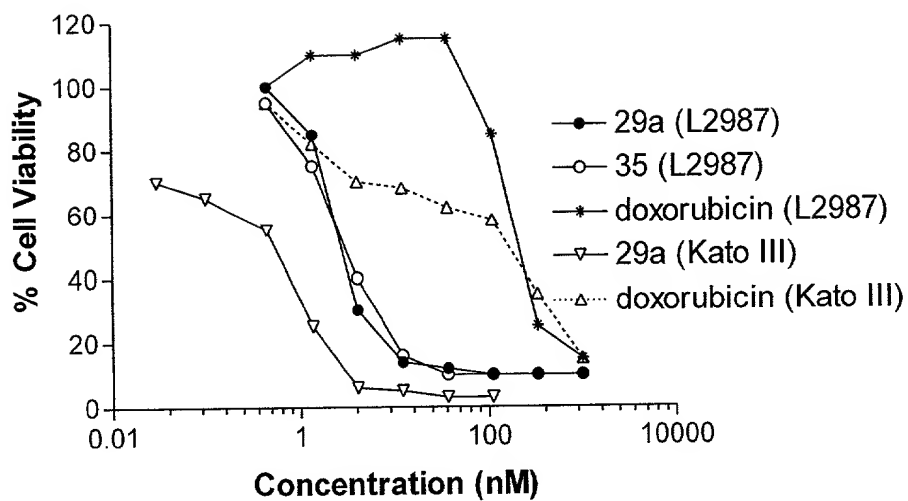
*Fig. 10*



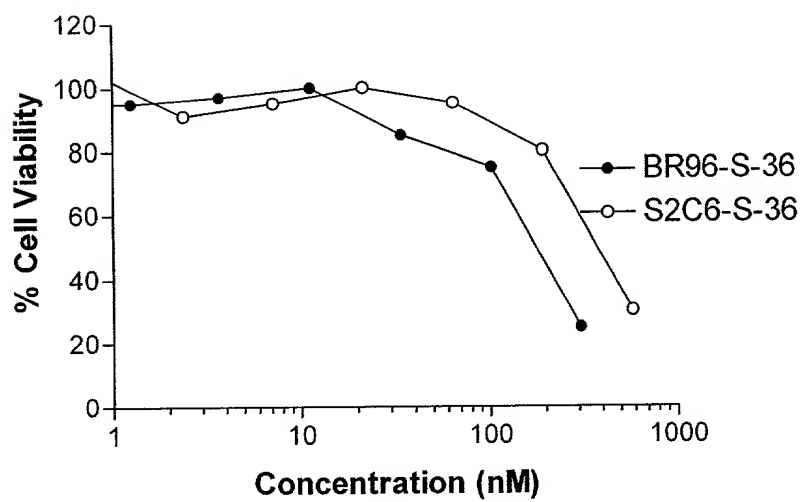
mAb-SH



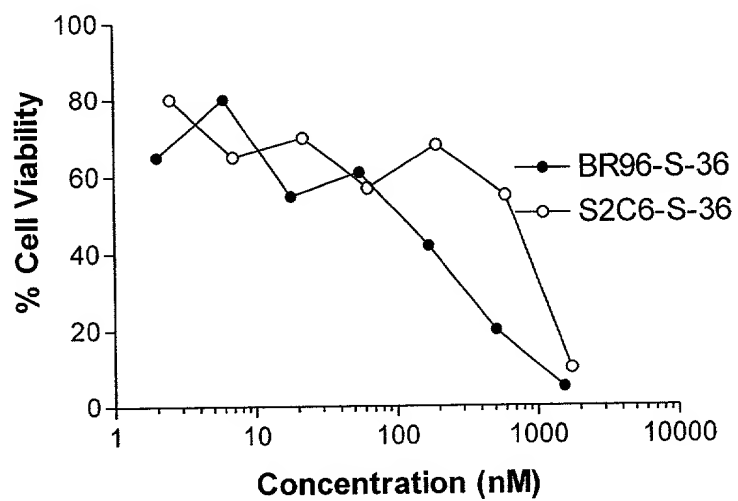
*Fig. 11*



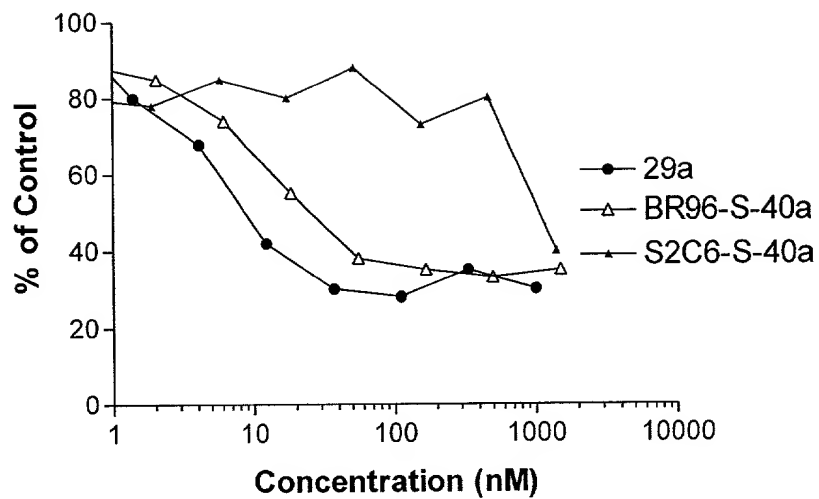
*Fig. 12A*



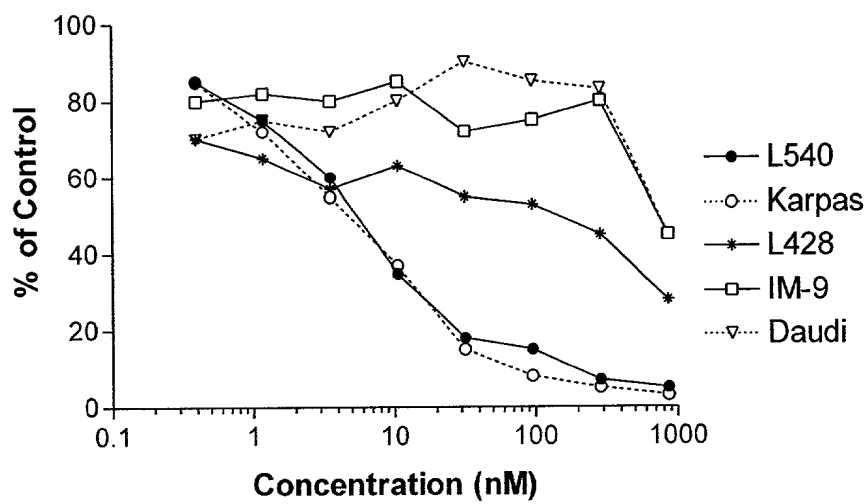
*Fig. 12B*



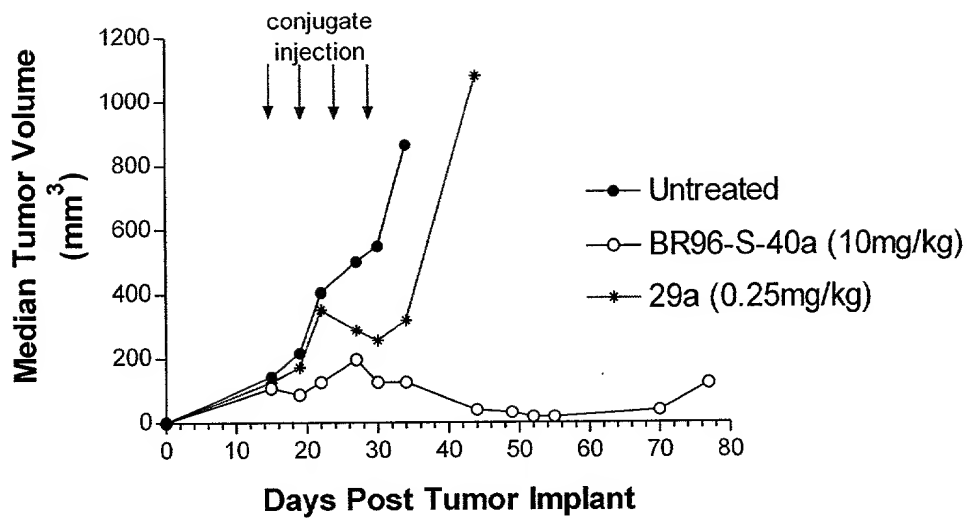
*Fig. 12C*



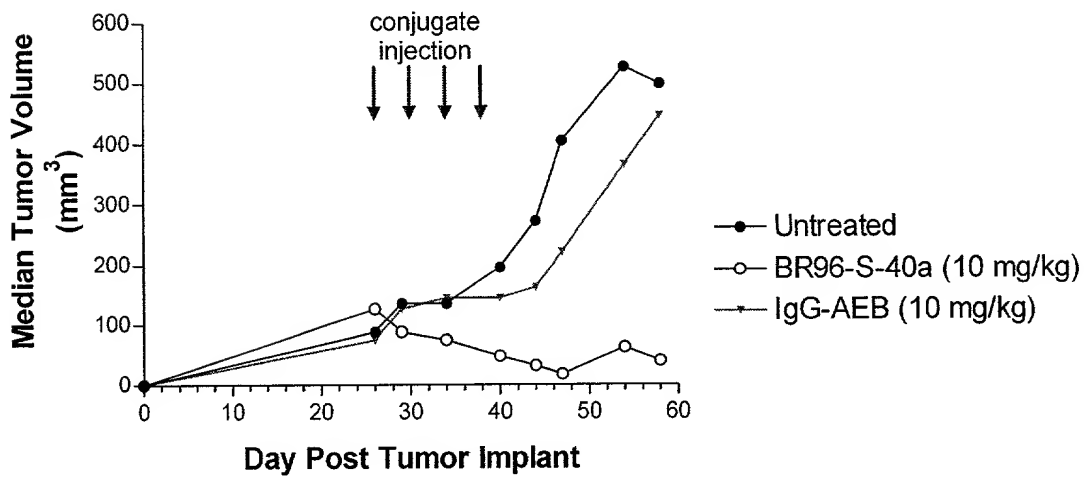
*Fig. 13A*



*Fig. 13B*



*Fig. 14A*



*Fig. 14B*